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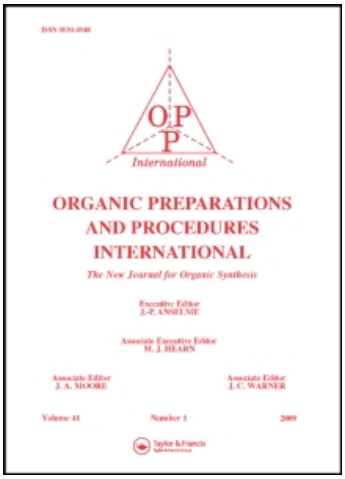

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SYNTHESIS OF NOVEL *meta*-BROMOPHENOLIC COMPOUNDS

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SYNTHESIS OF NOVEL *meta*-BROMOPHENOLIC COMPOUNDS

Submitted by (09/03/91)

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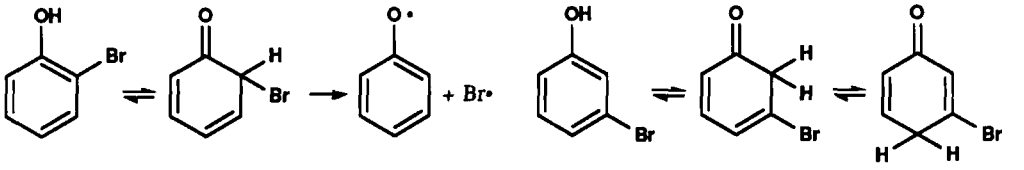
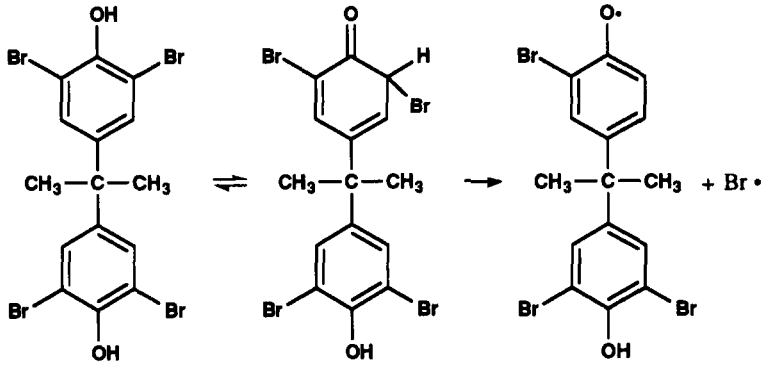
Tetrabromobisphenol-A (TBBA) and many other brominated phenolic compounds are widely utilized as a flame-retardant additives to impart a degree of ignition resistance to various polymers. These phenols containing bromine atoms *o*- or *p*- to a hydroxy group or a glycidyl ether group, have proven to be the cause of inferior thermal stability and wire bond failure for semiconductors.[1] We have reported[2] that *o*- and *p*-brominated phenols form an unstable cyclohexadienone structure *via* keto-enol tautomerization. Upon heating, this unstable cyclohexadienone structure generates bromine radicals, which in turn abstract a hydrogen from neighboring molecules to form HBr which

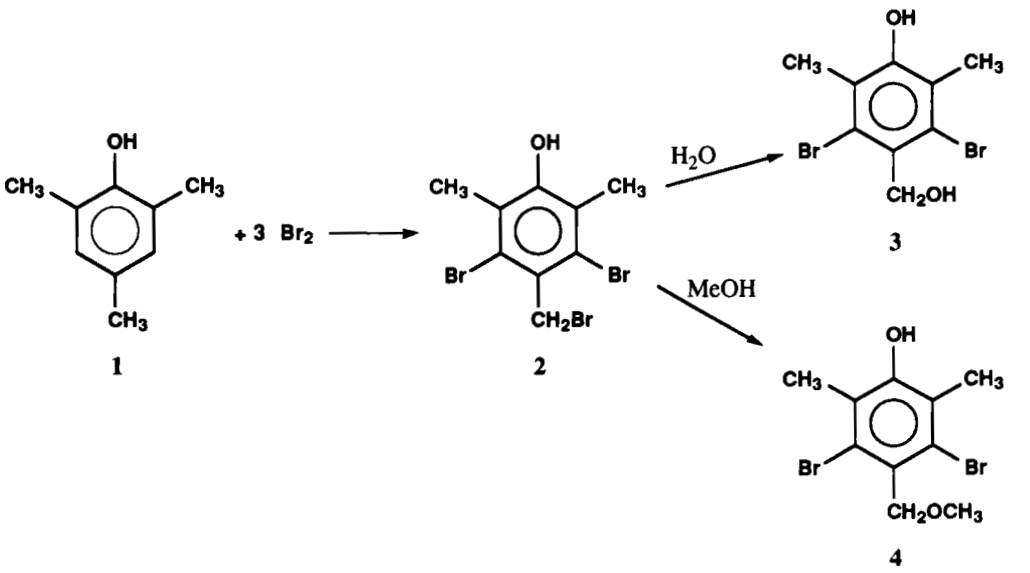


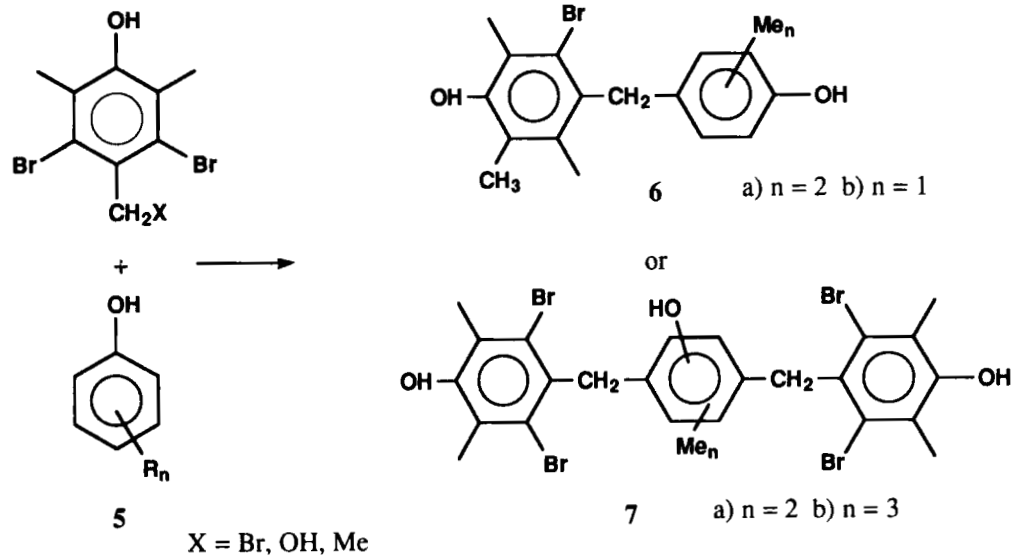
causes corrosion of bonding wire. *m*-Brominated phenols will not generate bromine radical as readily as *o*- or *p*-brominated phenols because of the location of bromine. This view was further demonstrated by the electron spin resonance (ESR) measurement of the free radical concentrations of *o*-brominated tetrabromobisphenol-A (TBBA) and the *m*-dibrominated 2,4,6-trimethylphenol after heating at 259° for1 hr. A relative radical concentration of 960 for TBBA to <10 for the *m*-dibrominated trimethylphenol was observed.



TBBA

Unfortunately, very few *m*-brominated bisphenols have been described. Auwer and Allendof[3] reported the preparation of 2,2',6,6'-tetrabromo-3,3',5,5'-tetramethyl-4,4'-dihydroxystilbene from 4-bromomethyl-3,5-dibromo-2,6-dimethylphenol. However, its extreme insolubility limits its use. Recently, various novel *m*-brominated bisphenols were synthesized for the development of stable brominated phenols for electronic application. It involves the bromination of 2,4,6-trimethylphenol (**1**) with excess bromine to produce 4-bromomethyl-3,5-dibromo-2,6-dimethylphenol (**2**)[4] as a major product. Hydrolysis or methanolysis of **2** produced 4-hydroxymethyl-3,5-dibromo-2,6-dimethylphenol (**3**) or 4-methoxymethyl-3,5-dibromo-2,6-dimethylphenol (**4**).





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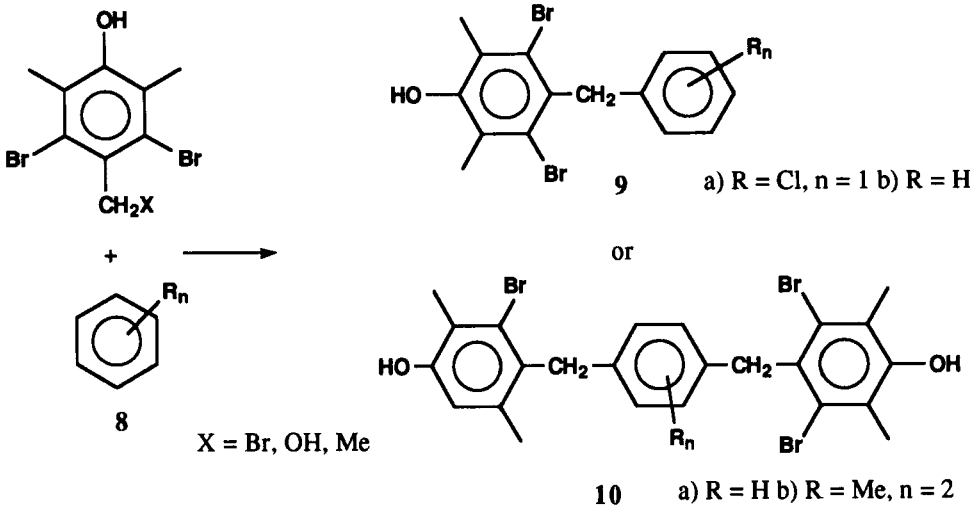
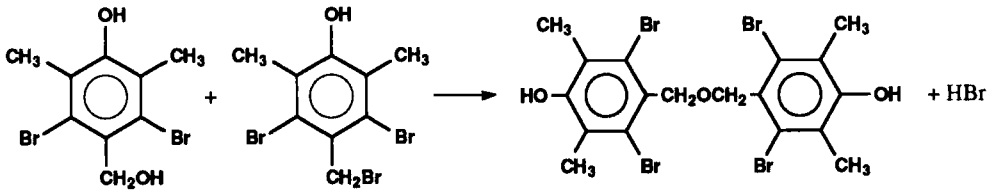


All three bromophenols (**2**, **3** and **4**) are excellent alkylating agents. With or without catalyst, they readily alkylate other phenols. They are such powerful alkylating agents that they alkylate *m*-position when the *o*- or *p*- position is substituted or even alkylate nonactivated aromatic compounds, such as benzene, chlorobenzene and *m*-xylene. In this fashion, eight novel metabromophenolic compounds were synthesized in excellent yields.

The novel 2,6-dibromo-3,5-dimethyl-4-hydroxybenzyl ether (**11**) was synthesized in one step by partial hydrolysis of 4-bromomethyl-3,5-dibromo-2,6- dimethylphenol (**2**) to 4-hydroxymethyl derivative (**3**) which then reacted with starting 4-bromomethyl compound (**2**) *in situ*.



In electronic encapsulation and laminate applications, the *m*-bromobisphenols synthesized above have exhibited superior hydrolytic and thermal stability as compared with the conventional *o*-brominated bisphenols. These properties have resulted in an extended device life for semiconductors and the printed circuit board, while meeting flame retardancy requirements as well.[5]

EXPERIMENTAL SECTION

All reagents and solvents were reagent grade or were purified by standard methods before use. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian EM-390 spectrometer. The mass spectra (MS) were

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taken on a Hewlett Packard 5985-A spectrometer. High Performance Liquid Chromatography (HPLC) and Gas Chromatography were performed on Shimadzu LC-9A and GC-14A. Microanalysis were performed on a Hewlett Packard Model 185B CHN analyzer.

Monoalkylation of 2,6-Dimethylphenol with 2.- To a 3 necked flask equipped with a stirrer, thermometer and reflux condenser, 37.3 g (0.10 mole) of 4-bromomethyl-3,5-dibromo-2,6-dimethylphenol (**2**), 12.2 g (0.1 mole) of 2,6-dimethylphenol, 0.015 g of ferric chloride and 300 mL of methylene chloride were added. The solution was gently heated to 40° over a period of 1 hr. Evolution of HBr gas was detected immediately and a precipitate began to form. The reaction mixture was further refluxed for 0.5 hr and then cooled to 25°. The solid was collected and dried in a vacuum oven to afford 37.3 g (90%) of **6a** as a white solid which was analyzed by gas chromatography to be 99+% pure, mp. 210-211°; MS (m/e) 414(M^+), ^{1}H NMR(acetone-d_6): δ 2.20 (s, 6H), 2.40 (s, 6H), 4.30 (s, 2H), 6.60 (s, 2H).

Anal. Calcd. for $C_{17}H_{18}Br_2O_2$: C, 49.28; H, 4.35; Br, 38.64. Found: C, 49.30; H, 4.31; Br, 38.60

Monoalkylation of 2,6-Dimethylphenol with 3.- To a 100 mL round-bottom flask equipped with a reflux condenser, stirrer and thermometer, was charged 6.2 g (0.02 mole) of 4-hydroxymethyl-3,5-dibromo-2,6-dimethylphenol (**3**), 2.44 g (0.020 mole) of 2,6-dimethylphenol and 25 mL of nitrobenzene. The mixture was heated to 175° with agitation over a period of 30 min. The temperatures was maintained at 175° for 1 hr and the reaction mixture was allowed to cool to room temperature. The resulted precipitate was collected and was dried over-night in a vacuum oven to give 66.8 g (82%) of **6a**, mp. 210-211°, undepressed by mixing with the sample prepared above. Liquid chromatographic and ^{1}H NMR analyses of the solid showed that the resulting product was identical with the one prepared above.

Monoalkylation of 2,6-Dimethylphenol with 4.- To a 250 mL round bottom flask equipped with a stirrer, thermometer and reflux condenser, 6.48 g (0.02 mole) of 4-methoxymethyl-3,5-dibromo-2,6-dimethylphenol (**4**), 2.44 g (0.02 mole) of 2,6-dimethylphenol, 100 mL of carbon tetrachloride and 0.2 g (0.001 mole) of *p*-toluenesulfonic acid were added. The mixture was heated to reflux and maintained at that temperature for 8.0 hrs. Methanol was produced as a by product. The reaction mixture was cooled to room temperature, insoluble solids were filtered and dried in a vacuum oven to give 6.3 g (76%) of **6a** in 99+% purity by gas chromatography, mp. 210-211°; ^{1}H NMR and elemental analyses were identical with the monoalkylated 2,6- dimethylphenol.

Monoalkylation of *o*-Cresol.- The typical procedure for alkylation was employed except *o*-cresol was used as a starting material instead of 2,6-dimethylphenol. Isolated solids (**6b**, 93%), mp. 197-199°; ^{1}H NMR (acetone-d_6): δ 2.20 (s, 3H), 2.40 (s, 6H), 4.30 (s, 2H), 6.60 (s, 2H), 6.80 (s, 1H).

Anal. Calcd. for $C_{16}H_{16}Br_2O_2$: C, 48.00 ; H, 4.00 ; Br, 40.00. Found: C, 48.11 ; H, 4.03; Br, 39.89

Dialkylation of *o*-Cresol.- The typical procedure was followed except 2:1 mole ratio of (**2**) to *o*-cresol was employed in the reaction. isolated solids (**7a**, 95%), analyzed by liquid chromatography, contained 96% dialkylated product, with 1% monoalkylated and 1% trialkylated *o*-cresol. mp. 224-

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226°; ^{1}H NMR (acetone-d_6): δ 2.20 (s, 3H), 2.30 (s, 6H), 2.40 (s, 6H), 4.20 (s, 2H), 4.40 (s, 2H), 5.80 (s, 1H), 6.80 (s, 1H).

Anal. Calcd. for $C_{25}H_{24}Br_4O_3$: C, 43.35; H, 3.47; Br, 46.24. Found : C, 43.38; H, 3.55; Br, 46.10

Dialkylation of 2,4,6-Trimethylphenol.- The typical procedure was followed except 2:1 mole ratio of **2** to 2,4,6-trimethylphenol was used in this reaction. Isolated solid (76%), analyzed by liquid chromatograpliy, contained 96% dialkylated product with 4% monoalkylated product. The solid was further purified by slurrying in hot methylene chloride followed by cooling to 25° and filtration to afford dialkylated product **7b** with 99% purity, mp. 164-166° ; ^{1}H NMR (acetone-d_6): δ 1.80 (s, 3H), 2.10 (s, 6H), 2.30 (s, 12H), 4.40 (s, 4H).

Anal. Cacld. for $C_{27}H_{28}Br_4O_3$: C, 45.00; H, 3.89; Br, 44.44. Found: C, 4.5.11; H, 3.92; Br, 44.32

Monoalkylation of Chlorobenzene.- The typical procedure was followed except 1:5 mole ratio of **2** to chlorobenzene was used as reactants. After the completion of HBr evolution, solvent and excess chlorobenzene were removed by a rotary evaporator under a reduced pressure. A brown oil was obtained which was recrystallized from hexane. It afforded a light tan solid (**9a**, 56%), MS (m/e) 404 (M^+); ^{1}H NMR ($CDCl_3$): δ 2.34 (s, 6H), 4.44 (s, 2H), 7.12 (m, 4H).

Anal. Cacld. for $C_{15}H_{13}Br_2ClO$: C, 44.50; H, 3.21; Br, 39.55; Cl, 8.78

Found: C, 44.58; H, 3.25; Br, 39.46; Cl, 8.72

Monoalkylation of Benzene.- The typical procedure was followed except 1:5 mole ratio of **2** to benzene was employed in the reaction. After removal of solvent and excess benzene by a rotary evaporator, (**9b**, 76%) was obtained. ^{1}H NMR ($CDCl_3$): δ 2.33 (s, 6H), 4.48 (s, 2H), 7.16 (m, 5H).

Anal. Calcd. for $C_{15}H_{14}Br_2O$: C, 48.65; H, 3.78; Br, 43.24. Found: C, 48.69; H, 3.80; Br, 43.21

Dialkylation of Benzene.- Compound **2** (112.0 g, 0.30 mole), 13.0 mL (0.150 mole) of benzene, 0.10 g (0.0006 mole) of anhydrous ferric chloride and 1.2 L of methylene chloride were added to a 2 L flask. The solution was heated to reflux with agitation and then maintained at reflux for 2.0 hrs. Precipitates formed during the refluxing period. The slurry was cooled to 25° and then filtered to afford 85.6 g white solid. The solid was further purified by slurrying in 250 mL of acetone for 1 hr, and then filtered. After drying in a vacuum oven, it afforded 81.7 g (96%) of **10a**. ^{1}H NMR (DMSO-d_6 + CCl_4 1:1): δ 2.31 (s, 2H), 4.34 (s. 4H), 6.92 (s, 4H).

Anal. Calcd. for $C_{24}H_{22}Br_4O_2$: C, 34.50; H, 3.32; Br, 48.34. Found: C, 43.55; H, 3.36; Br, 48.29

Dialkylation of *m*-Xylene.- The procedure for the dialkylation of benzene was used except benzene was replaced by *m*-xylene. It gave dialkylated product (**10b**, 79%) in 99+% puritv by liquid chromatography, mp. 295-297°; ^{1}H NMR (DMSO-d_6): δ 2.20 (s, 12H), 2.30 (s, 6H), 4.10 (s, 4H), 5.40 (s, 1H), 6.90 (s, 1H).

Anal. Cacld. for $C_{26}H_{26}Br_4O_2$: C, 45.22; H, 3.77; Br, 48.38. Found: C, 45.29; H, 3.80; Br, 48.31

2,6-Dibromo-3,5-dimethyl-4-hydroxybenzyl Ether (11).- A 373 g (1.0 mole) portion of **2** was dissolved in 750 mL of acetone. The solution was heated to reflux and 250 mL of water was added. A clear solution was obtained. The solution was refluxed for 5 hrs. A white precipitate formed during

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the refluxing period. The hot slurry was filtered to afford 184 g of white solid containing 97% ether and 3% **3** by liquid chromatography. The solid was further purified by slurring in 800 mLof acetone and 200 ml of water and refluxing for one-half hour. Hot filtration of the slurry produced **11** of 98+% purity with a mp. 240-241°. ^{1}H NMR (DMSO-d_6): δ 2.26 (s, 12H), 4.75 (s, 4H), 7.50 (s, 2H).
Anal. Calcd. for $C_{18}H_{18}Br_4O_3$: C, 35.88; H, 2.99; Br, 53.16. Found: C, 35.96; H, 3.01; Br, 53.03

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REDUCTION OF 3- AND/OR 5-UNSUBSTITUTED 2-ETHYLPYRAZOLIUM SALTS WITH COMPLEX METAL HYDRIDES. SYNTHESIS OF PYRAZOLIDINES

Submitted by (04/13/89) Luis A. Bañuelos, Purificación Cuadrado, Ana M. González* and Francisco J. Pulido

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Previous disclosures[1] described the regioselective synthesis of 3-pyrazolines by reduction of 1,3,5-trisubstituted 2-alkylpyrazolium salts with complex metal hydrides (CMH). The present investigation reports that the reduction of 3- and/or 5-unsubstituted 2-ethylpyrazolium salts with the same hydrides leads to results different from the above, giving pyrazolidines (**2**) as major products (Table 1).

The formation of pyrazolidines which does not depend of the molar ratio of hydride used,